

Claims

1. A peptide of least 9 amino acids in length derived from the tandem repeat domain of MUC1 and having the amino acid sequence SAP at its N-terminus.
2. The peptide of claim 1, essentially consisting of 10 to 25 amino acids.
3. The peptide of claim 1 or 2, which is a fragment of said tandem repeat domain, preferably peptide SAP17 (SEQ ID NO: 11).
4. The peptide of any one of claims 1 to 3, which comprises an amino acid sequence of any one of SEQ ID NOS: 1 to 4 or 11, or variants thereof, wherein said variants comprise one or more amino acid additions, insertions, substitutions and/or deletions as compared to the sequence of any one of SEQ ID NOS: 1 to 4 or 11, and wherein the biological activity is substantially equal to the activity of the peptide comprising the unmodified amino acid sequence of any one of SEQ ID NOS: 1 to 4 or 11.
5. The peptide of one or more of claims 1 to 4, wherein one or more of the threonines or serines of the peptide are O-glycosylated.
6. The peptide of claim 5, having an amino acid sequence of any one of SEQ ID NOS: 1 to 4 or 11, wherein the amino acid is glycosylated at Thr 5 and/or 12.
7. A nucleic acid encoding a peptide of any one of claims 1 to 6.
8. A method of producing a peptide of one or more of claims 1 to 6, comprising the following steps:
 - (a) providing a peptide comprising the tandem repeat domain of MUC1 or a part thereof, which part at least contains one repeating unit of said tandem repeat domain of MUC1;
 - (b) contacting the peptide of (a) with an effective amount of cathepsin-L or a closely related enzyme hereof, thereby cleaving the peptide; and
 - (c) isolating the fragments produced in (b).

9. The method of claim 8, wherein the peptide provided in step (a) is natural MUC1 derived from human milk fat membranes, from human tumor ascites or from human breast carcinoma cell lines or is represented by any one of SEQ ID NOS: 5, 6, 9, 10, or 12.
- 5
10. The method of claim 8 or 9, wherein one or more of the amino acids of the peptide provided in step (a) is O-glycosylated, provided that the peptide is not glycosylated at the cleaving site of cathepsin-L.
- 10 11. The method of any one of claims 8 to 10, wherein one or more of the threonines or serines of the peptide fragment isolated in (c) are O-glycosylated.
12. A peptide obtainable by a method of any one of claims 8 to 11.
- 15 13. A fusion molecule comprising the peptide of any one of claims 1 to 7 or 12.
14. An ex vivo-method of producing a population of autologous antigen presenting cells (APCs), which are capable of inducing effective immune responses against MUC1, comprising the steps of
- 20 (a) providing autologous APCs from a tumor patient;
- (b) contacting the autologous APCs from the tumor patient with an effective amount of a peptide or fusion molecule of any one of claims 1 to 6 or claim 12 to 13 under conditions which allow endocytosis, processing and MHC class II presentation of the peptide fragments by said APCs; and
- 25 (c) isolating said peptide presenting APCs for the purpose of immunotherapeutic application in the patient.
15. The method of claim 14, wherein the peptides in (b) are bound to ferric oxide beads.
- 30 16. An ex vivo-method of producing genetically engineered APCs, which are capable of inducing effective immune responses against MUC1, comprising the steps of
- (a) providing a nucleic acid encoding at least one peptide of any one of claims 1 to 6 or 12, or the fusion molecule of claim 13,
- (b) transfecting the APCs with said nucleic acid, and

(c) selecting APCs, which present said peptides in an MHC II restricted manner.

17. The method of claim 16, wherein the nucleic acid is provided in an expression vector in step (a).

5

18. An APC obtainable by the method of any one of claims 14 to 17.

19. The APC of claim 18, which is a dendritic cell or a B cell.

10 20. A composition comprising a therapeutically effective amount of the MUC 1 peptide of any one of claims 1 to 6 or claim 12, and/or the fusion molecule of claim 13 and/or the APCs of any one of claims 18 or 19; and optionally a pharmaceutically acceptable carrier.

15 21. The therapeutic composition of claim 20, which is a vaccine.

22. Use of a peptide of any one of claims 1 to 6 or 12, the nucleic acids of claim 7, the fusion molecule of claim 13, or the APCs of claims 18 or 19 for the preparation of a pharmaceutical composition for the treatment of MUC1-positive carcinomas.

20

23. The use of claim 22; wherein the MUC1-positive carcinoma is breast, colorectal, pancreatic and gastric cancer.

24. A method of treatment of patients suffering from a MUC1-positive carcinoma, wherein
25 the therapeutic composition of claim 20 is administered to the patient in an amount effective to induce an immune response against MUC1.

30